

# Limitations of the Classical Approach

“Historically, a serious limitation of NMR structure determination has been the inability of NMR to determine global conformations of macromolecules ... While NMR can precisely determine local structural features, errors tend to propagate through the length of the molecule. Thus if there are no NOE interactions between separate parts of a molecule, the long range conformation becomes poorly defined.”

Hansen, Mueller and Pardi, *Nature Structural Biology*, 5  
(1998) 1065-1074